REMARKS

In the present Amendment, claim 54 has been amended for clarification. No new matter has been added, and entry of the Amendment is respectfully requested.

Claims 1, 4, 6-11 and 13-54 are pending, of which claims 18-41 are withdrawn from consideration.

Response to § 112 Rejections

1. At page 2 of the Action, claim 54 is rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement.

The Examiner states that although there is support in the specification for the particulate portion to be made of monomers chosen from methyl methacrylate, methacrylate and styrene, there is no support in the specification for the particulate polymer portion to be composed of a mix of polymethylmethacrylate, polymethacrylate and polystyrene (polymers).

2. At page 2 of the Action, claim 54 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite.

The Examiner states that in claim 54, it is not clear whether Applicants want the particulate polymer portion to be made of a mix of the polymethylmethacrylate, polymethacrylate and polystyrene polymers or if Applicants want the polymer to be chosen from this group. The Examiner further states that since the former option does not have support in the specification as described above, for the purpose of further examination, this claim will be given the latter interpretation.

Claim 54 has been amended to recite that "the polymer in the said particulate polymer portion is selected from the group consisting of poly methyl methacrylate, poly methacrylate and polystyrene."

In view of the above, reconsideration and withdrawal of the §112 rejections are respectfully requested.

Response to §§ 102/103 Rejections

At page 3 of the Action, claims 1, 6, 16, 17, 43, 45-47, 49, 53 and 54 are rejected under 35 U.S.C. § 102(b) as being anticipated by or, in the alternative, under 35 U.S.C. § 103(a) as being obvious over Lidgren (US 6,586,009).

At page 4 of the Action, claims 4, 9-11, 42, 50 and 51 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Lidgren.

At page 4 of the Action, claims 7 and 8 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Lidgren, and further in view of Posey-Dowty et al. (US 5,258,420).

At page 5 of the Action, claims 13 and 15 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Lidgren, and further in view of Wenz (DE 20218668; citations are taken from the English language equivalent US 2005/0287071).

At page 5 of the Action, claims 14 and 52 are rejected under 35 U.S.C. §103(a) as being unpatentable over Lidgren, and further in view of Nies et al. (US 5,650,108).

All the above §§ 102/103 rejections should be withdrawn because the cited references do not disclose or render obvious the present invention, either alone or in combination.

As explained in the Amendment under 37 C.F.R. § 1.111 filed July 21, 2010, the organoiodine compounds of Lidgren do not dissolve in the liquid phase and cannot be incorporated in the particulate phase, as they are merely mixed with the polymer which is already in solid form. When the two phases are mixed to form a bone cement (Applicant notes that there is no actual example of this in Lidgren) the organoiodine compound would not dissolve because it is not soluble in either component. As explained in the second paragraph at page 2 of the

specification, agents such as iohexol and iodixanol, the preferred contrast agents of Lidgren, are known to have a negative impact on the mechanical properties of cements into which they are incorporated.

In contrast, the present invention provides a bone cement in which the organoiodine compound is dissolved/incorporated in at least one of the portions. When the monomer and polymer portions are combined to form a bone cement, the organoiodine compound is distributed homogenously throughout the cement. Moreover, as the organoiodine compound is dissolved/incorporated in one of the portions, it does not exist in particulate form.

As disclosed at the end of page 1 of the specification, the existence of insoluble particles of contrast agent in bone cements leads to reduction of strength of the cement. This problem is solved by the present invention which dissolves the contrast agent, thus ensuring that no particles exist to affect the mechanical characteristics of the bone cement. The cement of the present invention has superior strength, even at higher doses of contrast agent than those of Lidgren.

In order to demonstrate the unexpectedly superior results provided by the present invention and the patentability of the present claims over Lidgren and the cited secondary references, Applicants submit herewith a Declaration under 37 C.F.R. § 1.132 executed by Mr. Bjarne Brudeli.

In the Declaration, three groups of bone cements were prepared, one group containing iohexol hexaacetate (IHA, a contrast agent soluble in the cement according to the present invention) and further sets of cements containing iohexol (IHX) and iodixanol (IDX). IHX and IDX are contrast agents as suggested by Lidgren and are not soluble in bone cement, they therefore must be incorporated in the form of insoluble particles. The IHA cements, on the other hand, comprise IHA dissolved in one of the portions of the cement as required by the present

claims. The experiments were intended to demonstrate how the distinguishing feature of the present invention (the dissolved contrast agent) contributes to solving the problem of impaired mechanical properties.

As shown in Figure 1 at page 5 of the Declaration, the bone cements containing 20% IHA show significantly higher tensile strength than the IHX cement ($p<0.001$). Moreover, the strain at failure is significantly higher for the IHA cements when compared to the IHX cements ($p<0.00001$), see Figure 2 at page 6 of the Declaration.

As shown in Figure 3 at page 7 of the Declaration, the bone cements containing 20% IHA also show significantly higher tensile strength than the bone cements containing 13.75% IDX ($p<0.000001$). The strain at failure is also significantly higher for the IHA cement than for the IDX cement ($p<0.02$), see Figure 4 at page 8 of the Declaration. The IHA cement showed a 27 % higher maximum tensile strength than the IDX cement, and a 16 % higher strain at failure.

That is, the IHA cements which contain a dissolved organoiodine compound have improved mechanical properties over the cements suggested by Lidgren which contain particulate organoiodine compounds.

Further, the table at page 9 of the Declaration shows the concentration of contrast agent and iodine in each composition before addition of the equal amounts of monomer (20 mL of Palacos® R monomer liquid). The experiment was designed such that cements with comparable amounts of iodine were used. The IHA cements had slightly more iodine than the IHX and IDX cements, this meant that the IHA cements attenuate more X-rays and so were tested under a disadvantage, making the setup into somewhat of a worst case scenario for the IHA cements. As addition of contrast agent is known to weaken the resulting cement, the IHA compositions would be expected to perform worst in the strength tests due to their higher contrast agent content. The

results therefore show a surprising and significant improvement when the dissolved contrast agents according to the present invention are used.

In summary, bone cement containing IHA according to the present invention shows significantly superior mechanical properties than bone cements containing IHX or IDX, even at higher contrast media contents.

The present invention relates to monomer/polymer soluble iodinated X-ray contrast agents in bone cement where the contrast agent is dissolved in the cement. Incorporation of the contrast agent into the monomer and/or polymer portion of the cement reduces the negative influence (reduction of mechanical strength and increased risk of loosening) of the contrast agent in the final bone cement. Because the organoiodine compound is dissolved in one of the portions, the bone cement has increased mechanical strength as shown by the experiments in the Declaration. Incorporation of a dissolved contrast agent into the monomer and/or polymer portion is neither taught nor suggested by the prior art, therefore, the claims are patentable over the prior art.

In view of the above, reconsideration and withdrawal of all the §§102/103(a) rejections based on the cited references are respectfully requested.

Allowance is respectfully requested. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,

Susan J. Mack
Registration No. 30,051

SUGHRUE MION, PLLC
Telephone: (202) 293-7060
Facsimile: (202) 293-7860

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